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Placental Hofbauer cells assemble and sequester HIV-1 in tetraspanin and DC SIGN positive compartments that are accessible to neutralizing antibodies

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Background

Within monocyte derived macrophages, HIV-1 accumulates in virus containing compartments (VCCs) that are largely inaccessible to the external environment, which implicate these cells as HIV-1 reservoirs. During mother to child transmission, placental macrophages (Hofbauer Cells [HCs]) are viral targets, and have shown to be infected *in vivo* and sustain low levels of viral replication *in vitro*, however, the risk of *in utero* transmission is less than 7%. The role of these primary macrophages as viral reservoirs is largely undefined.

Methods

With consent, term placentas from 20 HIV-1 seronegative women were obtained following caesarian section. VCCs were evaluated with 3D confocal microscopy and correlated with electron microscopy. Co localization R values (Pearson's correlation) were quantified with co localization module of Volocity5.2.1. Replication kinetics following siRNA and neutralization studies were evaluated using p24 ELISA.

Results

We demonstrate primary HCs assemble and sequester HIV-1 in VCCs with localization specific to intracellular vesicles and the plasma membrane. These compartments are enriched in endosomal/lysosomal markers, including CD9, CD81, CD63 and LAMP 1, along with DC SIGN. Following internalization, we observed HIV-1 accumulation in acidified compartments. Remarkably, these compartments are accessible via the cell surface and can be targeted by exogenously applied small molecules and HIV-1 specific neutralizing antibodies (NAbs). In addition, broadly NAbs (4E10 and VRC01) neutralized HIV-1 infected HCs and involve the participation of FcγRI for inhibition.

Conclusion

These findings suggest placental HCs possess intrinsic adaptations facilitating sequestration of HIV-1, and may serve as a protective viral reservoir to permit viral degradation, neutralization and antiretroviral drug entry *in utero*.

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